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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:			
CAJACOB, *et al.*		Art Unit:	1631
Appln. No.:	09/233,218	Examiner:	Y. Kim
Filed:	January 20, 1999	Atty. Docket:	16517.231
For:	Nucleic Acid Molecules and Other Molecules Associated with the Tetrapyrrole Pathway		

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Notice of Appeal from the Examiner to the Board of Patent Appeals and Interferences

Commissioner for Patents
Washington, DC 20231

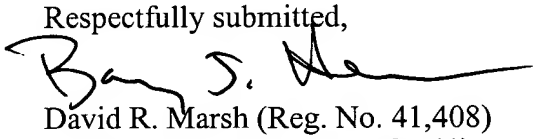
Sir:

Applicants hereby appeal to the Board of Patent Appeals and Interferences from the decision of the Examiner mailed December 17, 2001, that resulted in Applicants having claims that have been twice or finally rejected.

Check number 153739 submitted herewith includes payment of the fee of $ 320.00 for filing a Notice of Appeal from the Examiner to the Board of Patent Appeals and Interferences (37 C.F.R. § 1.17(b)). In the event that extensions of time under 37 C.F.R. § 1.136 other than those otherwise provided for in the papers accompanying this Notice are required to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 50-1824 referencing docket number 16517.231 / 38-21(15090)B. A duplicate copy of this Notice is attached.

Respectfully submitted,



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#21 Appeal Brief

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:			
Claire A. CAJACOB *et al.*		Art Unit:	1631
Appln. No.:	09/233,218	Examiner:	Y. Kim
Filed:	January 20, 1999	Atty. Docket:	16517.231/38-21(15090)B
For:	Nucleic Acid Molecules and Other Molecules Associated with the Tetrapyrrole Pathway		

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APPELLANT'S BRIEF

Commissioner for Patents
Washington, DC 20231

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-described patent application. A Notice of Appeal was filed on March 15, 2002. The statutory fee of $320.00 for submitting this Brief is included in our attached Check No. **159117**. *This Brief is submitted in triplicate.*

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167. Monsanto Company is a subsidiary of Pharmacia Corporation, located at 100 Route 206 North, Peapack, New Jersey 07977.

2. Related Appeals and Interferences

The Applicants are unaware of any Appeals or Interferences related to this Appeal.

3. Status of Claims

Claims 1, 2, and 10-21 are pending. Claims 3-9 were withdrawn from consideration by the Examiner, and are not under appeal. Claims 1, 2, and 10-21 stand finally rejected under 35 U.S.C. § 112, first paragraph, and claims 11-21 additionally stand finally rejected under 35 U.S.C. § 101. Applicants appeal all of the rejections of claims 1, 2, and 10-21.

4. Status of Amendments

Applicants have not filed any responses subsequent to the Final Office Action mailed December 17, 2001, in this case.

5. Summary of Invention

The invention is directed to nucleic acid molecules that encode a maize or soybean tetrapyrrole pathway enzyme, and in particular a glutamyl-tRNA reductase enzyme, or fragments thereof. Specification at page 23, line 9 through page 24, line 15. More specifically, the present invention is directed to nucleic acid molecules that comprise a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605. Specification at page 67, lines 18-20, Table A.

6. Issues

The issues in this Appeal are:

(a) whether claims 11-21 are unpatentable under 35 U.S.C. § 101 for allegedly being unsupported by a specific asserted utility or a well established utility;

(b) whether claims 11-21 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because the claimed invention purportedly lacks utility;

(c) whether claims 1, 2, and 10 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement; and

(d) whether claims 1, 2, and 10-21 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged insufficiency of written description.

7. Grouping of Claims

The patentability of claims 11-21 is addressed in Section 8.B below. The patentability of all claims is addressed in section 8.C through 8.D below. A copy of the claims on appeal is attached hereto as Appendix A.

8. Argument

A. Summary of Applicants' Position

As the Supreme Court said in *Brenner v. Manson*, the "basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility....where specific benefit exists in currently available form." 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Applicants have met this part of the bargain – they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example use to encode a glutamyl-tRNA reductase enzyme ("Glu TR") or a fragment thereof. This benefit is specific, not vague or unknown, and it is a "real world" or substantial benefit. Because the claimed nucleic acids provide at least this benefit, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed nucleic acids for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112, first paragraph, has been met.

Furthermore, Applicants have provided an adequate description of the claimed nucleic acids that demonstrates Applicants' possession of the claimed invention. Each genus of claimed nucleic acid molecules, *i.e.*, the nucleic acid molecules that encode Glu TR, and more specifically, those comprising the nucleic acid sequences of SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605, has been described by the recitation of a common structural feature – the nucleotide sequences of SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605, respectively – which distinguishes molecules in the genus from molecules not in the claimed genus. Because the specification demonstrates that Applicants have possession of (and

have provided an adequate description of) the claimed genus of nucleic acid molecules, the specification satisfies the written description requirement of 35 U.S.C. § 112, first paragraph.

B. The Claimed Nucleic Acids Have Legal Utility

Pending claims 11-21 were erroneously rejected under 35 U.S.C. § 101 because the claimed inventions were allegedly not supported by either a "substantial utility" or a "specific asserted utility." Final Office Action mailed December 17, 2001 (Paper No. 19) ("Final Action") at pages 2-3. According to the Final Action, the asserted utilities of the claimed nucleic acid molecules are not persuasive because "the claims are not drawn to a glutamyl tRNA reductase but a nucleic acid sequences comprising the claimed SEQ ID Numbers" and because of the "unreliability in assigning proteins' functions strictly based in their degree homology". Final Action at page 2.

The Examiner's analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson.* The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide <u>one</u> identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

The courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*,

51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Applicants have asserted in the specification that the claimed nucleic acid molecules provide identifiable benefits, for example use to identify the presence or absence of a polymorphism, and use as a hybridization probe for expression profiling. *See, e.g.*, specification at page 52, line 3 through page 53, line 5; page 83 line 9 through page 91, line 3; and page 91, lines 4 to 13. Either of these utilities alone is enough to satisfy Section 101. Therefore, Applicants need not rely solely on the use of the disclosed SEQ ID Nos to encode Glu TR, or fragments thereof, to prove the utility of the claimed invention. Because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

(1) The Claimed Nucleic Acid Molecules Provide A Specific Benefit, *i.e.*, They Have Specific Utility

Applicants have asserted that the claimed nucleic acid molecules[1] are themselves useful for utilities disclosed in the specification, *e.g.*, to detect the presence or absence of polymorphisms, and as hybridization probes for expression profiling. The specification also discloses additional utilities for the claimed nucleic acid molecules, including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to overexpress a desired protein. Specification at page 108, line 6

[1] It is irrelevant whether the corresponding mRNA or polypeptide have utility because Applicants are not relying on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules.

through page 109, line 3. For example, a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored. Such a screen is analogous to a cell-based assay, which has a legally sufficient utility.[2] Thus, the use in such a screen of a plant or plant cell having an introduced claimed nucleic acid molecule is a legally sufficient utility. Other utilities disclosed in the specification include use of the claimed nucleic acid molecules to measure the level of mRNA in a sample,[3] and use as molecular markers.[4]

The Examiner has likewise acknowledged that these and several other uses are disclosed and described in the specification. *See* Office Action of August 30, 2000 (paper number 11), at page 6. Any of these utilities alone is enough to satisfy Section 101. Because Applicants need only establish a single utility to satisfy 35 U.S.C. §101, and they have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

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[2] *See, e.g.*, MPEP § 2107.01 at page 2100-32.

[3] It is standard practice to screen populations of nucleic acids with EST sequences, often attached to a microarray, without characterizing each and every target mRNA. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. For example, such information is useful to detect expression changes in traits of interest, *e.g.*, drought stress. Contrary to the Examiner's assertions, this use is not using the claimed nucleic acid molecules to identify "real world applications." *See* Office Action mailed July 16, 2001, at page 3. It is a **use** of the claimed nucleic acid molecules in a real world context.

[4] One can use the claimed nucleic acid molecules to determine location of a corresponding DNA sequence on a physical map or genetic map location without knowing anything beyond the claimed sequence. The use of molecular markers is a practical activity in the development of nutritionally enhanced or agriculturally enhanced crops. Such markers are useful in, for example, genetic mapping or linkage analysis, marker-assisted breeding, physical genome mapping, transgenic crop production, crop monitoring diagnostics, and gene identification and isolation. As more markers are identified, genetic maps will become more detailed and it will be easier for plant breeders to breed for particular traits.

(a) Identifying the Presence or Absence of a Polymorphism

One of the utilities disclosed in the specification is use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism. Specification at page 83, line 9 through page 91, line 3. The Examiner argues that this utility, like all of the asserted utilities, is not specific or substantial, *see* Office Action of July 16, 2001 (paper number 17), at pages 3-4, but does not provide any support (legal or factual) for the proposition that detection of polymorphisms is not a legal utility.

Many of the disclosed utilities in this case, including this utility, are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell, or organism. The Examiner denigrates this utility by asserting that these uses are not "useful" because they are not specific and "applicable to any nucleic acids in general". Office Action mailed July 16, 2001, at page 3. However, the fact that, for example, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds)." MPEP § 2107.01 at page 2100-33.

Use of the claimed nucleic acid molecules to detect the presence or absence of polymorphisms is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.[5] Likewise, the claimed nucleic acid molecules

[5] For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled "Chlorine Specific Gas Chromatographic Detector."

have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usefully demonstrates that the two (or more) populations being compared share a common genetic heritage.

The claimed nucleic acid molecules have been asserted to work for a specific, *i.e.*, not vague or unknown benefit – to identify the presence or absence of a polymorphism. This benefit is immediately realized directly from the use of the claimed nucleic acids, not from the use of other molecules. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Probes for Other Molecules or Source for Primers

Other uses for the claimed nucleic acid molecules are as probes for other molecules or as a source of primers. The Examiner suggests that these uses are not legal utilities because the "the nucleic acids are not disclosed as being useful as probes for detecting a specific condition, primers for amplifying a target region which would serve as an indication of some condition, etc." Office Action of July 16, 2001, at page 3. This is not correct. The specification discloses that the claimed nucleic acid molecules can be used, via hybridization, in real world applications such as to isolate nucleic acid molecules of other plants and organisms such as alfalfa, *Arabidopsis*, barley, *Brassica*, broccoli, cabbage, etc.[6] Specification at page 80, line 17 through page 81 line 9. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and so has not met the burden of proof required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

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[6] Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Applicants to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed nucleic acid molecules.

One illustrative example of a molecule that can be isolated using the claimed nucleic acid molecules is the promoter of the gene corresponding to the claimed nucleic acid molecules. Applicants have specifically disclosed that one use of the claimed nucleic acid molecules is to initiate a chromosome walk. Specification at page 82, line 5 through page 83, line 8. The Examiner denigrates that utility when he asserts that it is not specific to a particular nucleic acid. Office Action February 1, 2001 (paper number 15), at page 3; Office Action of July 16, 2001, at page 3.

In short, the Examiner appears to be arguing that the utility is not a legal utility simply because other molecules can be used for the same purpose, *i.e.*, chromosome walks. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not "specific" to the claimed nucleic acids. The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in the tetrapyrrole pathway of a maize or soybean plant. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a <u>better</u> starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules. An invention may be "less effective than existing

devices but nevertheless meet the statutory criteria for patentability." *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the claimed nucleic acid molecules could not be so used. Accordingly, the assertion of this utility as a probe for other molecules or as a source of primers satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

(2) The Claimed Nucleic Acid Molecules Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

It appears that the Examiner is arguing that the disclosed uses are legally insufficient or "insubstantial" under 35 U.S.C. § 101, but such an argument has no basis in law. The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). "'Practical utility' is a shorthand way of attributing 'real world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) ("tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use").[7]

There can be no question that one skilled in the art can use the claimed nucleic acid molecules in a manner which provides an immediate benefit to the public, for example to detect the presence or absence of polymorphisms. The detection of polymorphisms provides an immediate benefit to the public because, for example, it enables a plant breeder to determine the distribution of parental genetic material in the progeny of a cross. This information about a

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[7] *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

plant's genetic profile, like the information about a compound's pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

Quite apart from the detection of polymorphisms, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed "real world" value to such nucleic acid molecules. The utility of ESTs is not merely an academic issue; the real world value of ESTs is self-evident from the growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs. Like fermentation processes involving bacteria, ESTs and nucleic acid molecules with EST sequences are "industrial product[s] used in an industrial process – a useful or technical art if there ever was one." *See, e.g., In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The market participants for EST products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to pay for useless inventions. *Compare Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983) ("People rarely, if ever, appropriate useless inventions"). Quite simply, the commercial value of ESTs is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

(3) The Nucleic Acid Sequences Encode the Polypeptides Described in the Specification

The Final Action, at pages 2-3, asserts that the claimed nucleic acid sequences do not meet the utility requirement because there is allegedly no evidence that the nucleic acid sequences encode a polypeptide that has the same function as GluTR. In support of this position, the Office Action of July 16, 2001 provides references that corroborate the unreliability in assigning proteins' functions based on their degree of homology. In response, Applicants submit

the following articles where sequence similarity is routinely used by those of ordinary skill in the art as a predictor of function. *See, e.g.,* Venter, *et al.*, The Sequence of the Human Genome, *Science, 291*: 1304-1351 (2001); Woese, *et al.*, Conservation of Primary Structure in 16S rRNA, *Nature, 254*: 83-85 (1975). Accordingly, Applicants maintain that one of ordinary skill in the art would have recognized, in light of the specification's teachings, that at the time of filing Applicants had possession of the claimed invention for the uses described in the specification.

Furthermore, as the Final Action acknowledges, the claims are directed to nucleic acid sequences comprising the claimed SEQ ID NOs and not to a glutamyl tRNA reductase. *See* Final Action at page 2. The utility of the claimed nucleic acid molecules to encode a glutamyl tRNA reductase enzyme is only one of the stated utilities disclosed in the specification. Applicants have disclosed several uses for the claimed SEQ ID NOs, described above. Any single one of these uses satisfies the utility requirement of 35 U.S.C. § 101.

(4) The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 706.03(a). Cases in which utility was found not to be credible are rare, and usually involve "hare-brained" utilities.[8] A challenge to the credibility of a utility is essentially a challenge directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead

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[8] Examples of incredible utilities are given in MPEP § 2107.01 at page 2100-34, and include:

> an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 706.03(a)(1).

Applicants has explicitly identified specific and substantial utilities, not only in the specification, but in Applicants' Response of April 23, 2001, at page 5 and in the Response of October 4, 2001, at page 3. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). Unless and until the Examiner can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

C. The Claimed Nucleic Acids Are Enabled by the Specification

The enablement of the claimed nucleic acid molecules has been challenged. Claims 11-21 were erroneously rejected as not enabled by the specification, because the claimed nucleic acid molecules allegedly lack utility and therefore cannot be enabled. Final Action at page 3. This rejection has been overcome by the arguments stated above regarding utility because it is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

Claims 1, 2, and 10 were also erroneously rejected as not being enabled by the specification. The Final Action maintains the enablement rejection imposed in the Office Action

of July 16, 2001 at pages 4-7. The Examiner asserts "[t]he previous Office Action clearly set forth many conditions that resulted in the undue experimentation determination". Final Action at page 4.

Applicants have previously responded to the Examiner's analysis of the Wands factors set forth in the Office Action of July 16, 2001 at pages 4-7. Applicants maintain that a reasonable analysis of the *In re Wands* criteria supports Applicants position that no undue experimentation would be required to make and use the claimed invention. *See In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1998).

The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, *e.g.*, of conservative nucleotide substitutions, identification of an active site, and radiometric synthase assay conditions, to which a person of ordinary skill in the art has access. Performing routine and well-known steps, such as sequence alignment protocols, molecular weight determination, and antibody hybridization assays, cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 218-219 (C.C.P.A. 1976).

Moreover, the specification provides evidence based on sequence identity (Table A) that the disclosed genes encode polypeptides having GluTR activity. Furthermore, the specification teaches that the deduced amino acid sequence of GluTR from all species exhibit about 60% overall similarity with stretches of amino acid identity. In particular, barley, *Arabidposis*, and cucumber exhibit over 70% identity at the deduced amino acid level. *See* Specification at page 5. Further, the specification teaches that GluTR generally has a molecular weight of about 270 kD among species. *See id.* at page 4. As such, it is submitted that sequence homology is indeed an adequate and predictable indicator of GluTR functionality. As such, one of ordinary skill in the art would clearly understand from the teachings of the specification that the claimed nucleic acid sequences have GluTR activity without the need for undue experimentation.

The second and third *Wands* criteria relate to the amount of direction or guidance given, and the presence or absence of working examples. Again, the specification provides evidence of sequence identity, discloses a general range of molecular weight, and discusses the use of GluTR specific antibodies. Based on such disclosure, one of ordinary skill in the art would be enabled to make and use the invention commensurate in scope with the claims.

The fourth, fifth, and sixth *Wands* criteria focuses on the nature of the invention, the state of the art, and the relative skill in the art. The present invention relates to nucleic acid and amino acid sequences, and constructs and methods related thereto. Practitioners in this art are guided by considerable knowledge and resources on the conditions and approaches that can be utilized to identify, confirm, and introduce into other hosts, nucleic acid and amino acid sequences.

The seventh criterion considers the predictability of the art. The Office Action of July 16, 2001, alleges that "the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function." Office Action of July 16, 2001, at page 6. Applicants respectfully disagree and assert, as discussed *supra*, that the specification discloses sufficient guidance to render the results predictable.

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). In the present case, one of skill in the art is specifically guided by the disclosure to look to, *e.g.*, sequence identity data, molecular weight data, and antibody binding, in making that determination.

Accordingly, for at least these reasons, the enablement rejection under 35 USC § 112, first paragraph, is improper and must be reversed.

The Final Action further argues that the specification "did not demonstrate that the proteins encoded by the claimed nucleic acids had the same function [as GluTR]". Final Action at page 4. The Final Action submits in support of this allegation that the references disclosed in the Office Action of July 16, 2001, at page 6, demonstrate "the unreliability in assigning proteins' functions strictly based on their degree homology" and shifts the burden to Applicants to provide evidence to the contrary. Final Action at page 5.

Applicants believe the references cited in Section 8.B.3 above establish that sequence similarity is routinely used by those of ordinary skill in the art as a predictor of function. This evidence, in addition to the analysis of the Wands factors, discussed *surpa*, conclusively establishes that one of ordinary skill in the art would be able to make and use the claimed invention based on the disclosure in the specification.

D. The Specification Provides An Adequate Written Description of the Claimed Invention

Despite the Examiner's admission that SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605 are adequately described by the specification (*see* Office Action of February 1, 2001, at page 5), the adequacy of the written description of the claimed invention has been challenged by the Examiner because the nucleic acid molecules of all of the claims are allegedly "not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s)...had possession of the claimed invention." Final Action at page 5. The bases for the Examiner's challenge are apparently that (1) one of skill in the art would allegedly conclude that Applicants was not in possession of the claimed nucleic acid molecules, and (2) there is allegedly an insufficient written description to support the genus encompassed by the claim. Final Action at pages 5-6. These are not proper bases for a written description rejection of a "comprising" claim. If they were, every "comprising" claim ever written would be invalid for failing to describe every nuance of the claimed invention. Furthermore, the specification

demonstrates to one skilled in the art that Applicants were in possession of the claimed genera of nucleic acid molecules.

(1) The Specification Reflects Applicant's Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if not every nuance, then the written description has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. A person of ordinary skill in the art, *e.g.*, a molecular biologist, would, after reading the present specification, understand that Applicants had possession of SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, 605, and their complements, and therefore, the claimed invention.

Applicants has provided the nucleotide sequences required by the claims, *e.g.*, SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605, polypeptides encoded by these and other disclosed nucleic acid molecules, vectors comprising these nucleotide sequences, and bacterial artificial chromosomes comprising these nucleotide sequences, and have thus established possession of the claimed invention. The fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences, or that hybridize under specific conditions to the recited sequences does not mean that Applicants were any less in possession of the claimed nucleic acid molecules.[9] It is well-established that use of

[9] If the Examiner is arguing that no possession is shown because the precise claim language is not used in the specification, then it goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498,

the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986).

The present application describes more than just the nucleotide sequence required by the claims (*e.g.*, SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605), for example, it describes enzymes encoded by the nucleic acids of the present invention (specification at page 23, line 9 through page 31, line 4; at page 73, line 3 through page 75, line 2; and Table A) and vectors comprising the claimed nucleic acid molecules (specification at page 36, line 7 through page 40, line 6, and page 109, line 4 through page 118, line 9). Furthermore, the addition of extra nucleotides or detectable labels to the disclosed nucleotide sequences (SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605) is readily envisioned by one of ordinary skill in the art upon reading the present specification,[10] in particular at page 58, lines 19-23 (describing sequences with labels to facilitate detection), page 75, line 12 through page 76, line 14 and page 77, lines 1-8 (describing fusion nucleic acid molecules), and page 161 line 22 through page 163, line 6 (citing references describing the construction, manipulation and isolation of nucleic acid macromolecules).

(2) Applicants Has Described the Claimed Invention

The Examiner asserts that Applicants have allegedly not satisfied the written description requirement because it is "not apparent from the specification that it disclosed the full open

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1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972).

[10] It is established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques." *E.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

reading frame of the claimed nucleic acids." Final Action at page 6. The Final Action relies on Example 7 of the Written Description Training Material in support of this rejection.[11] The Examiner appears to assert that each nucleic acid molecule within the claimed genus must be described by its complete structure. Final Action at page 6. These assertions are totally unfounded. The Federal Circuit has elucidated a test for written description wherein a genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Applicants have satisfied that test for written description.

The claimed nucleic acid molecules are a genus of nucleic acid molecules, each genus having a common structural feature of a particular enumerated nucleotide sequence, *i.e.*, SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605. The respective common structural feature (the nucleotide sequence) is shared by every nucleic acid molecule in the claimed genus, and it distinguishes the members of the claimed genus from non-members. For example, if a nucleic acid molecule such as an mRNA contains the nucleotide sequence of SEQ ID NO: 586, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 586. If a nucleic acid molecule does not contain SEQ ID NO: 586, then it is not a member of that claimed genus. The presence of other nucleotides at either end of the recited sequence will not interfere with the recognition of a claimed nucleic acid molecule as such – it either contains the nucleotides of SEQ ID NO: 586 or it does not.[12] One skilled in the

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[11] Applicants respectfully point out that the Patent Office has said the examples in the Written Description Guidelines "only describe how to determine whether the written description requirement of 35 U.S.C. 112, para. 1 is satisfied. Regardless of the outcome of that determination, Office personnel must complete the patentability determination under all the relevant statutory provisions of Title 35 of the U.S. Code." Written Description Training Material at pages 4-5. *See also Request for Comments on Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112(1) 'Written Description' Requirement*, 63 Fed. Reg. 32639, 32639-44 (June 15, 1998). As such, the Examiner's sole reliance on the Guidelines (Final Action at 6) is improper.

[12] The same argument applies to each of the other genera, for example, if a fusion construct contains the nucleotide sequence of SEQ ID NO: 600, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 600.

art would clearly know if a nucleic acid molecule contains one of the recited nucleotide sequences. Thus, claims 2 and 10-21 satisfy the written description requirement of 35 U.S.C. § 112, and the rejection should be reversed.

Moreover, Applicants have also disclosed and described numerous additional nucleotide sequences which encode maize or soybean tetapyrrole pathway enzymes and fragments thereof. *See, e.g.,* specification at page 23, line 9 through page 31, line 4; page 65, line 15 through page 68, line 16; and Table A. From this disclosure in the specification, one of ordinary skill in the art would readily recognize that Applicants had possession of a substantially purified nucleic acid molecule that encodes a maize or soybean tetrapyrrole pathway enzyme or fragment thereof, and particularly a glutamyl-tRNA reductase enzyme. Thus, claim 1 satisfies the written description requirement of 35 U.S.C. § 112, and the rejection should be reversed.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,

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APPENDIX A

1. A substantially purified nucleic acid molecule that encodes a maize or soybean tetrapyrrole pathway enzyme or fragment thereof, wherein said maize or soybean tetapyrrole pathway enzyme is a glutamyl-tRNA reductase enzyme.
2. The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605.

10. The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule comprises a nucleic acid sequence having between 100% and 90% identity with a sequence selected from the group consisting of SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605.
11. A substantially purified nucleic acid molecule, comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605.
12. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 586.
13. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 590.
14. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 594.
15. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 596.
16. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 597.
17. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 599.
18. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 600.
19. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 601.
20. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 604.
21. The nucleic acid molecule of claim 11, wherein said sequence is SEQ ID NO: 605.